

REMARKS

Claims 2-17 and 56-58 were pending in the present application. Claims 1 and 18-55 were previously cancelled. By virtue of this response, no claims have been cancelled, claims 2, 12, and 58 have been amended, and new claim 59 has been added. Accordingly, claims 2-17 and 56-59 are currently under consideration. Allowance of the pending claims is respectfully requested.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim amendments

Claims 2, 12, and 58 have been amended and new claim 59 added by virtue of this Amendment.

Claim 2 has been amended to recite that the method comprises designating (a) a first quantitative lipid metabolite profile from a first biological sample and (b) a second quantitative lipid metabolite profile. The claim has been further amended to recite that the method comprises identifying differences or similarities in a plurality of *individual* lipid metabolites between the first and second quantitative lipid metabolite profiles. Support for these amendments is found, e.g., in lines 16-19 at page 37, line 17 at page 12 to line 23 at page 13, lines 8-11 at page 9, and line 33 at page 25 to line 25 at page 26, as well as throughout the application as filed.

Claim 12 has been amended to recite that the method for generating the lipid metabolite profiles comprises measuring the quantities of a plurality of individual lipid metabolites in the fractions. Support for this amendment is found, e.g., in lines 2-5 at page 9 and lines 15-26 at page 10, as well as throughout the application as filed.

Minor amendments have been made to claim 58 to make the language of claim 58 consistent with the language of amended claim 2.

Support for new claim 59 is found, e.g., in lines 16-19 at page 37, line 17 at page 12 to line 23 at page 13, lines 8-11 at page 9, and lines 16-19 at page 10, as well as throughout the specification.

No new matter is added by these amendments.

Claim Rejections under 35 U.S.C. § 102

Claims 2, 3, 5, 6, 12 and 56-58 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ruan et al. (Journal of Dairy Science, volume 81, 1998, pages 9-15). In the rejection, the Examiner indicated his belief that Figure 5 of Ruan et al. illustrates a heat map. Applicants respectfully traverse this rejection.

As amended, independent claim 2 is directed to a method for presenting analysis of quantitative lipid metabolite profiles, comprising: designating (a) a first quantitative lipid metabolite profile from a first biological sample and (b) a second quantitative lipid metabolite profile; identifying differences or similarities in a plurality of individual lipid metabolites between the first and second quantitative lipid metabolite profiles; and displaying the identified differences or similarities on a heat map. Dependent claim 3 states that each quantitative lipid metabolite profile comprises quantitative measurements of at least two lipids and wherein the quantified measurements are obtained using an internal standard for at least one of the lipids. Dependent claim 5 states that the quantitative lipid metabolite profiles each comprise a quantified measurement of a lipid in a lipid class. Dependent claim 6 states that the quantified measurement of the lipid in the lipid class is obtained using an internal standard for the lipid class. Dependent claim 12, as amended, states that at least one of the quantitative lipid metabolite profiles is generated using a method comprising: separating a biological sample into fractions based on a plurality of lipid classes, wherein at least one quantitative internal standard is included for each lipid class; and measuring the quantities of a plurality of individual lipid metabolites in the fractions. Claim 56 recites that an increase or decrease in the lipid metabolite is indicated on the heat map by a color and the relevant amount of the increase or decrease is indicated by the intensity of the color. The

method of dependent claim 57 further comprises generating a written report. Dependent claim 58, as amended, states that the second quantitative lipid metabolite profile is a control lipomic profile.

To anticipate a claim, a prior art reference must teach or suggest each and every limitation of the claim. Applicants respectfully submit that the Ruan et al. reference does not anticipate claims 2, 3, 5, 6, 12 and 56-58, because the reference fails to disclose or suggest all elements of claims 2, 3, 5, 6, 12 and 56-58.

For instance, the Ruan et al. reference does not teach or suggest any methods involving a quantitative lipid metabolite profile from a *biological* sample. One skilled in the art would not consider a fabricated emulsion of Crisco oil in water as is disclosed in Ruan et al. to be a “biological sample,” especially in light of the teachings of Applicants’ specification regarding biological samples. See, e.g., the teachings regarding biological samples in the specification in line 36 at page 5 to line 4 at page 6, lines 3-31 at page 14, and line 33 at page 25 to line 25 at page 26, as well as elsewhere in the specification.

Furthermore, the reference Ruan et al. does not disclose the identification of differences or similarities in a *plurality* of *individual* lipid metabolites between the first and second quantitative lipid metabolite profiles. The compositions shown in Figures 5a and 5b comprise only water and Crisco oil. With regard to Figure 5b, the Examiner admits that water is not a lipid but remarks that “in a binary mixture of water and oil, the concentration of water is directly and uniquely dependent on the amount of oil added (the volume of the mixture not occupied by water can only be occupied by oil).” Nevertheless, even if the measure of water in a binary mixture is an indirect measure of the amount of oil, such a measure would simply be a different way of measuring the same oil that was being measured directly in Figure 5A, not a measure of a second lipid metabolite. The Examiner has further remarked that “Crisco is inherently a mixture of many lipids found in vegetables (i.e. vegetable oil is inherently not composed of a single oil or lipid).” This may be true, however, nowhere does Ruan et al. disclose the analysis of any *individual* lipid metabolites, let alone the analysis of a *plurality* of such individual lipid metabolites.

In addition, the Ruan et al. reference does not disclose the display of identified differences or similarities *on* a heat map. The Examiner points to the equations 1 and 2 shown on page 12 of Ruan et al., but even if equations 1 and 2 show the correlation between image intensity with the concentration of oil (or water) in the binary mixture, this correlation is not displayed on Figure 5 of Ruan et al., the figure which the Examiner is asserting is a heat map. Figure 5 shows the image density of the amount of Crisco oil or water measured in each sample and each sample is labeled with the theoretical amount of Crisco oil or water present, but the differences or similarities between the measured amount of Crisco oil or water and the theoretical amount is not identified and displayed in Figure 5 and neither are the difference or similarities between the measurements from the images in Figure 5A versus the measurements from the images in Figure 5B.

With respect to the rejection of claim 3, Applicants additionally contend that the Ruan et al. reference fails to teach or suggest the use of an internal standard. Even if the Ruan et al. reference shows measurements for samples in which it was predetermined that there was 0% Crisco oil or 100% Crisco oil, this does not mean that an internal standard has been used in any of the tested samples shown in Figure 5. One of ordinary skill in the art would recognize that an “internal standard” has to be “internal” to the sample being analyzed.

With respect to the rejection of claim 5, the examiner has not provided *any* support for his assertion that claim 5 is anticipated by the cited reference and therefore the rejection of claim 5 over Ruan et al. is improper. Furthermore, the Ruan et al. reference does not in fact teach or suggest the quantified measurement of an individual lipid in a lipid class. Even if the Ruan et al. reference does teach the measurement of the amount of Crisco oil in a sample, Crisco oil is, as the Examiner has indicated, a mixture of oils. Nowhere does the Ruan et al. reference teach or suggest, for example, the measurement of a lipid in a lipid class. Thus, claims 5 and 6 are not anticipated by the Ruan et al. reference.

With respect to the rejection of claim 6, Applicants contend that the Ruan et al. references fails to teach the use of an internal standard. As already noted above, even if the Ruan et al. reference shows measurements for samples in which it was predetermined that there was 0%

Crisco oil or 100% Crisco oil, this does not mean that an internal standard has been used in any of the tested samples shown in Figure 5. One of ordinary skill in the art would recognize that an “internal standard” has to be “internal” to the sample being analyzed.

In the rejection of claim 12, the Examiner states that “Figure 5 of Ruan et al. illustrates the biological samples separated into fractions where water is the standard against which the lipid classes are measured.” Applicants respectfully disagree. Applicants contend that nowhere does the Ruan et al. reference teach the use of lipid metabolite profiles generated by the separation of a biological sample into fractions based on a plurality of lipid classes. The samples pictured in Figure 5 which contain no oil or no water are not fractions of a biological sample. Ruan et al. does not teach that these 100% oil or water samples were ever derived from a mixture. See the paragraph “Oil-in-water emulsions” in the Materials and Methods section on page 10 of Ruan et al. which describes how the samples that were measured were made. Furthermore, as already discussed above with respect to the rejection of claim 6, the reference Ruan et al. does not disclose the use of an internal standard. In addition, the reference Ruan et al. does not teach the measurement of the quantities of a plurality of individual lipid metabolites.

With respect to the rejection of claim 58, Applicants respectfully contend that, despite the Examiner’s assertions, Ruan et al. does not teach or suggest the use of a control lipomic profile.

In light of the foregoing remarks, Applicants respectfully request that the rejection of claims 2, 3, 5, 6, 12 and 56-58 under 35 U.S.C. § 102(b) be withdrawn.

Claim Rejections under 35 U.S.C. § 103

Rejection #1 under 35 U.S.C. § 103:

Claims 15 and 16 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ruan et al. in view of Moser et al. (Moser et al., *Annals of Neurology*, volume 45, 1999, pages 100-110). Applicants respectfully traverse this rejection.

Claims 15 and 16 are dependent claims that depend from claim 12 and claim 2 and incorporate all elements of those claims. As discussed above with respect to the rejection of claim 2 and claim 12 under 35 U.S.C. 102, the reference Ruan et al. does not teach or suggest every element of claims 2 and 12. The combination of Moser et al. with Ruan et al. likewise does not teach or suggest every element of dependent claims 15 and 16.

In light of the foregoing remarks, Applicants respectfully request that the rejection of claims 15 and 16 under 35 U.S.C. § 103 be withdrawn.

Rejection #2 under 35 U.S.C. § 103:

Claims 7, 9, and 13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ruan et al. in view of Watkins et al. (Journal of Lipid Research, volume 39, 1998, pages 1583-1588). Applicants respectfully traverse this rejection.

Claims 7 and 9 are dependent claims that depend from claims 2 and 5, and incorporate all elements of those claims. Claim 13 is a dependent claim that depends from claims 2 and 12. As discussed above with respect to the rejection of claims 2, 5, and 12 under 35 U.S.C. 102, the reference Ruan et al. does not teach or suggest every element of claims 2, 5, and 12. The combination of Watkins et al. with Ruan et al. likewise does not teach or suggest every element of dependent claims 7, 9, and 13.

In light of the foregoing remarks, Applicants respectfully request that the rejection of claims 7, 9, and 13 under 35 U.S.C. § 103 be withdrawn.

Rejection #3 under 35 U.S.C. § 103:

Claims 4 and 14 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ruan et al. in view of Watkins et al. in view of Siguel (U.S. Patent No. 5,075,101). Applicants respectfully traverse this rejection.

Dependent claim 4 incorporates all elements of claims 2 and 3. Dependent claim 14 incorporates all elements of claims 2 and 12. As discussed above with respect to the rejection of claims 2, 3, and 12 under 35 U.S.C. 102, the reference Ruan et al. does not teach or suggest every element of claims 2, 3, and 12. The combination of Siguel with Ruan et al. likewise does not teach or suggest every element of dependent claims 4 and 14.

In light of the foregoing remarks, Applicants respectfully request that the rejection of claims 4 and 14 under 35 U.S.C. § 103 be withdrawn.

Rejection #4 under 35 U.S.C. § 103:

Claim 17 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ruan et al. in view of “The World of Membrane Lipids,” (www.biochem.Missouri.edu/~lesa/LIPIDS/membrane_lipid.html). Applicants respectfully traverse this rejection.

Dependent claim 17 incorporates all elements of claim 2. As discussed above with respect to the rejection of claim 2 under 35 U.S.C. 102 over Ruan et al., the reference Ruan et al. does not teach or suggest every element of claim 2. The combination of “The World of Membrane Lipids” with Ruan et al. likewise does not teach or suggest every element of dependent claim 17.

In light of the foregoing remarks, Applicants respectfully request that the rejection of claim 17 under 35 U.S.C. § 103 be withdrawn.

Rejection #5 under 35 U.S.C. § 103:

Claim 10 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ruan et al. in view of Grav et al. (Journal of Chromatography B, volume 658, 1994, pages 1-10). Applicants respectfully traverse this rejection.

Dependent claim 10 incorporates all elements of claims 2, 5, and 6. As discussed above with respect to the rejection of claims 2, 5, and 6 under 35 U.S.C. 102 over the reference Ruan et al., the reference Ruan et al. does not teach or suggest every element of claims 2, 5, and 6. The combination of Grav et al. with Ruan et al. likewise does not teach or suggest every element of dependent claim 10.

In light of the foregoing remarks, Applicants respectfully request that the rejection of claim 10 under 35 U.S.C. § 103 be withdrawn.

Rejection #6 under 35 U.S.C. § 103:

Claim 8 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ruan et al. in view of Dutta et al. (JAOCS, volume 74, no. 6, 1997, pages 647-657). Applicants respectfully traverse this rejection.

Dependent claim 8 incorporates all elements of claims 2 and 5. As discussed above with respect to the rejection of claims 2 and 5 under 35 U.S.C. 102 over the reference Ruan et al., the reference Ruan et al. does not teach or suggest every element of claims 2 and 5. The combination of Grav et al. with Dutta et al. likewise does not teach or suggest every element of dependent claim 8.

In light of the foregoing remarks, Applicants respectfully request that the rejection of claim 8 under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 475512000100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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